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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/558,741	04/26/2000	James S. Huston	PP0926.105	1163

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EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 09/12/2002

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/558,741

Applicant(s)

HUSTON ET AL.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33 and 97-100 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33 and 97-100 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 33, 97-100 are pending and under examination.
Claims 33, and 97-100 have been amended.
2. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Information Disclosure Statement

3. The IDS filed 5/30/00 has been partially considered with respect to all U. S. Patents, however, all other documents have not been considered because the cited references were not in 08/462,641. The IDS has been placed in the file and if Applicants would supply a copy of the references, they will be considered at that time. The response filed 3/5/02 states that copies of the references are enclosed. The references were not located and the Examiner apologizes but requests that the references be supplied again.

Rejections Withdrawn

4. The rejection of claims 34, 97-100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

Response to Arguments

Specification

5. The disclosure is objected to because of the following informalities:

a. The attempt to incorporate subject matter into this application by reference to sections in U.S. Patent 5,091,513 and to Figures 1a and 2A-D (now figures 7 and 8A-D) is improper because to incorporate material by reference, the host document / application must identify with detailed particularity what specific material it incorporates and clearly indicate where the material is found in the various documents. See Advanced Display Systems, Inc. v. Kent State Univ., 54 USPQ2d 1673 (Fed. Cir. 2000) citing In re Seversky, 177 USPQ 144, 146 (CCPa 1973). On page 26 of the instant application the specification recites "A detailed description for engineering and producing sFv proteins by recombinant means appears in US Patent 5,091,513 claiming priority from U.S.S.N. 052,800, filed May 21, 1987, assigned to Creative BioMolecules, Inc., hereby incorporated by reference.", however, the material added by the amendment of 10/01/01 contains the summary of the invention as well as descriptions of terms and what other regions the BABS can comprise such as fusion proteins and hinge regions (column 11-12) as well as the advantages of BABS (see column 7-8 of 5,091513). Also Figure 1A and 2A-D do not relate to sFv, they relate to fusion proteins and Fv and VH fusion proteins.

The response filed 3/5/02 has been carefully considered but is deemed not to be persuasive. The response states "so all agree that applicants evidenced an intent to incorporate that patent **in its entirety**." In response to this argument, the specification as stated above only intended to incorporate a detailed description of engineering and producing sFV proteins by recombinant means, not the reference in its entirety. As stated above other portions of the patent have been added to the instant application which do not relate to the engineering and production of sFV proteins. Applicants are pointed the case law of In re Seversky, 177 USPQ 144, 146 (CCPa 1973).

6. The rejection of claims 33 and 97-100 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 3/5/02 has been carefully considered but is deemed not to be persuasive. The response states that support for the claimed subject matter can be found at page 4 and page 5 (see response of 3/5/02). In response to this argument, the recited passages are not on the cited pages because the amendment filed 10/01/01 added the incorporated material to page 6, therefore the cited passages are not on pages 4-5. Even if the cited passages were found at the recited pages, the information which is claimed to support the instant claims is in the material that was incorporated, it is still not clear where support for all of the claimed limitations are found in the

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specification as originally filed. In addition, the cited pages 10, lines 2-8, 20-29, page 14, 25 to page 15, line 2 does not support the claimed invention. It is requested that a substituted specification be provided that contains the incorporated material and specific locations in the specification prior to and after incorporation that support the claimed invention.

7. The rejection of claims 98 and 100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

The response filed 3/5/02 has been carefully considered but is deemed not to be persuasive.

The response states that applicants disclosure in light of that which is known in the art and the specification provides ample support for the claimed invention (see page 9 of response) and the claims are directed to single polypeptide chain that can be immunoreactive with an antigen (see page 10 of response).

In response to these arguments, as evidenced from Rudikoff et al (which was not addressed in the response) an antigen binding site must comprise the CDRs and framework in a specified order. Thus even though one can screen for antigen binding it would require undue experimentation to determine which CDRs or which CDR residues to change and still retain antigen binding. In addition, it is not routine in the art to

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replace some of the CDR regions which encompasses replacing residues in the CDRs and it is not routine to determine which CDRs or residues to replace with human residues. In addition claim 100 still encompasses replacing any variable domain sequence which includes the CDRs with any human immunoglobulin sequence.

8. The rejection of claims 33 and 97, 99 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 9-12 of U.S. Patent No. 5,091,513 (IDS #3) in view of Jones et al (Nature 321:522, 1986) is maintained.

The response filed 3/5/02 has been carefully considered but is deemed not to be persuasive. The response states that applicants will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter. In response to this argument, no terminal disclaimer has been supplied and as such the rejection is maintained.

9. The rejection of claims 33, 97 and 99 under 35 U.S.C. 103(a) as being unpatentable over Klausner (BioTechnology 4:1041 and 1043, 12/86) and further in view of Pastan et al (Cell 47:641-648, 12/86) and Jones et al (Nature 321:522-525, 5/1986) is maintained.

The response filed 3/5/02 has been carefully considered but is deemed not to be persuasive. The response states "Applicants point out that the claims are directed not to a single chain antibody cross-linked or coupled to an additional moiety such as an

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immunotoxin or targeting moiety, but to a single chain antibody wherein the additional moiety is part of said single polypeptide chain" (see page 11 of response). In response to this argument, the claim recite that part (b) in claim 33 be "a part of said polypeptide chain" and as such Pastan et al teach a crosslinked moiety to an antibody. Thus, the moiety is part of the single polypeptide chain and has biological activity. In addition, the argument seems to ague the references separately in that Pastan does not teach a single chain antibody and Pastan does not teach a single chain antibody wherein the additional moiety is part of the single chain polypeptide. In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Thus, It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an immunotoxin comprising a single chain antibody as taught by Klausner and a toxin as taught by Pastan et al and humanize it as taught by Jones et al.

Conclusion

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

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Respectfully,

Larry R. Helms Ph.D.

703-306-5879


SHEELA HUFF
PRIMARY EXAMINER